based upon the restriction requirement and reserve all rights associated therewith under 35 U.S.C 121 and 37 C.F.R. 1.141-1.146.

In the prior application, Applicants canceled claims 1, 3, 4, 9, and 10 without prejudice and added new claims 17-25. The Examiner withdrew claims 5-8 and 11-16. Accordingly, in this application, claims 2 and 17-25 are pending.

Claims 2, 17, 18, 19, 22, and 23 were amended to more clearly and distinctly claim the invention. New claims 26-36 have been added. Support for the amendments and new claims can be found throughout the specification, including, e.g., page 4, line 8, through page 5, line 24; page 9, lines 8-12; and pages ~~26-32.~~ pages 26 - 32.

Neither the amendments nor the new claims incorporate new matter into the application or what would have been new matter in the prior application.

The following remarks discuss the amendments and address rejections made in the prior application in an Office Action dated January 17, 2001. In that Office Action, the Examiner made the following rejections/objection:

(a) Claims 2, 17, 22, 24, and 25 were rejected under 35 U.S.C. 112, first paragraph, as lacking antecedent basis;

(b) Claims 2 and 17-25 were rejected under 35 U.S.C. 102(b) as being anticipated by pir62 Accession No. S03013;

(c) Claims 2, 17-20, and 22-24 were rejected under 35 U.S.C. 102(b) as being anticipated by pir65 Accession No. S00524; and

(d) Claim 2 was objected to as depending from a previously canceled base claim.

A. **Rejections under 35 U.S.C. 112**

Claim 2 has been amended by deleting the phrase "partial modification thereof, or an allelic mutant." Claim 22 has been amended to delete the phrase "complement system inhibiting", for which the Examiner found no support in the specification. These amendments

render the previous Section 112 rejections moot.

In paragraph 6, the Examiner rejected claims 2, 17, 22, 24, and 25 for exceeding the scope of the disclosure. The Examiner contended that the claims encompass complement factor H from species, other than human or rat, that are not adequately described in the specification. The Examiner also contended that the specification fails to identify definitive structural features of the claimed genus.

Applicants respectfully traverse this rejection. Applicants cite the following four references-- all predating the priority date of November 28, 1996 -- which point out that as of the priority date, a person or ordinary skill in the art would have had sufficient knowledge to visualize or recognize the identity of members of the genus. The references are attached as Exhibits 1-4.

(1) Ripoche J, Day AJ, Harris TJ, and Sim RB. The complete amino acid sequence of human complement factor H. Biochem J. 1988, Jan. 15; 249(2): 593-602. PMID: 2963625.

(2) Kristensen T and Tack BF. Murine protein H is comprised of 20 repeating units, 61 amino acids in length. Proc Nat'l Acad Sci U.S.A. 1986 June; 83(11): 3963-7. PMID: 2940596.

(3) Dahmen A, Kaidoh T, Zipfel PF, and Gigli I. Cloning and characterisation of a cDNA representing a putative complement-regulatory plasma protein form barred sand bass (*Parablax neblifer*). Biochem J. 1994, July 15; 301 (Pt. 2): 391-7. PMID: 8042982.

(4) Soames CJ, Day AJ, and Sim RB. Prediction from sequence comparisons of residues of factor H involved in the interaction with complement component C3b. Biochem J. 1996, April 15; 315 (Pt. 2): 523-32.

PMID: 8615824.

These references 1-4 show that, before the priority date, complement factor H was known and sequenced for humans, mice, sea bass, and bovines, respectively. The second paragraph of the "Introduction" of Soames *et al.* cites four additional references (5-8) which disclose that factor H had also been isolated from rat, guinea pig, rabbit, and pig. Abstracts of these references are attached as Exhibits 5-8.

References 5-8 are as follows:

(5) Daha MR, van Es LA. Isolation, characterisation and mechanism of action of rat beta 1H. J. Immunol. 1982 April; 128(4):1839-43. PMID: 6460912.

(6) Horstmann RD, Muller-Eberhard DJ. Isolation of rabbit C3, Factor B, and factor H and comparison of their properties with those of the human analog. J. Immunol. 1985 Feb.; 143(2):1094-100. PMID: 3155535.

(7) Hogasen K, Jansen JH, Mollnes TE, Hovdenes J, Harboe M. Hereditary procine membranoproliferative glomerulonephritis type II is caused by factor H deficiency. J. Clin. Invest. 1995 March; 95(3):1054-61. PMID: 7883953.

(8) Bitter-Suermann D, Burger R, Hadding U. Activation of the alternative pathway of complement; efficient fluid-phase amplification by blockade of the regulatory complement protein beta1H through sulfated polyanions. Eur. J. Immunol. 1981 April; 11(4):291-5. PMID: 6454580.

Soames *et al.* also confirms the common structural arrangement of complement control protein modules, abbreviated as "CP," in factor H from <u>any</u> species. It states that:

> "Each CP is approximately 60 amino acids long and has a framework of four conserved cysteines, disulphide linked together in the pattern Cys1-Cys3 and

Cys2-Cys4." (Page 523, column 1, last sentence of second paragraph under "Introduction.")

Ripoche *et al.,* reference 1 above, shows this repeating structure in Figure 3 (page 599) and describes the structure as being

"... arranged in 20 homologous repeating units, each about 60 amino acids long, based on a framework of four invariant cysteine residues..." (Page 599, left column.)

Kristensen *et al.,* reference 2 above, states that

"Murine H was composed of 20 repetitive units, each about 61 amino acid residues in length." (See Abstract.)

Similarly, Dahmen *et al.*, reference 3 above, shows the repetitive SCR structure in Figure 3 and states that:

"Alignment of these SCRs (Figure 3) showed the organization of SBP1 into 17 SCRs, each containing four typical cysteine residues (C)". (Page 394, first paragraph under "Structural Analysis and Homology.")

Thus, these references confirm that as of the priority date, factor H and its structure were known from a variety of species. Applicants submit that these references recite a representative number of species, defined by a sequence, that fall within the scope of the claimed genus. The references also recite structural features common to members of the genus, which features are not just a substantial portion of the genus but, in fact, the whole of the genus. Because, as of the priority date, persons of ordinary skill in the art clearly knew and understood what factor H was, the specification does not require further description. The name of the genus "factor H" is, by itself, sufficient description of that material.

Therefore, based on the foregoing, at the priority date, those of ordinary skill in the art would have understood that the invention does, in fact, extend to the claimed genus. Thus, the specification supports the claims.

B. **Rejections under 35 U.S.C. 102(b)**

In paragraphs 7 and 8 of the previous Office Action, the Examiner rejected claims 2 and 17-25 as being anticipated by pir 62 Accession No. S03013, which is the Ripoche *et al.* reference cited above. In paragraph 9, the Examiner rejected claims 2, 17-20, and 22-24 as being anticipated by pir65 Accession No. "No. S00524 (Dec. 31, 1993)." Applicants assume that "S00524" is a typographical error and the Examiner meant Accession No. S00254, which is the same Ripoche *et al.* reference. Applicants address this rejection based on that reference.

Applicants respectfully traverse this rejection on the ground that the reference, Ripoche *et al.*, does not teach, suggest, or disclose the invention recited in the amended claims. Applicants' claims are directed to a truncated recombinant factor H and, more particularly, complement control protein modules 1-4, 1-5 or 1-6 of complement factor H.

By contrast, the reference teaches the entire sequence of human complement factor H and compares the human sequence to corresponding regions of mouse factor H cDNA. The reference explains that human factor H isolated from "outdated plasma" lacks two residues (Lys-Arg) from the C-terminus of the sequence. (Page 598, last paragraph, to page 599.) Though brief, this explanation of why a mere two amino acids may be missing from a sequence of 1,213 amino acids underscores the focus of this reference as being on the "entire" factor H sequence as a contiguous unit -- and not on discrete constituents.

Moreover, in the amino acid sequence disclosed in Figure 3, there is no indication of which amino acids correspond to complement control protein modules or even what those protein modules may be. Nor is there any indication of where one complement control protein module ends and the next begins. In fact, nowhere in the reference is there any disclosure concerning complement control protein modules -- in this case, modules 1-4, 1-5 or 1-6 – as having complement inhibiting activity, apart from the rest of the sequence. Nor does the reference disclose constructs having CCP modules of complement factor H.

For a reference to be anticipatory, it must sufficiently describe the claimed invention to have placed the public in possession of it. *See. E.g., In re Brown*, 329 F.2d 1006, 1011, 141 U.S.P.Q. 245, (C.C.P.A. 1964). That is, the reference must "clearly and unequivocally disclose

the claimed compound or direct those skilled in the art to the compound without any need for picking, choosing, and combining various disclosures." *In re Arkley*, 455 F.2d 586, 587, 172 U.S.P.Q. 524, 526 (C.C.P.A. 1972). Here, the Ripoche *et al.* reference fails to be "so particular and definite that from it alone, without experiment or the exertion of his own inventive skill, any person versed in the art to which it appertains could construct and use [the claimed invention]." *In re Brown,* 329 F.2d at 1011. Therefore, Applicants respectfully submit that their claimed invention is novel and patentable over Ripoche *et al.*

C. **Objection to Form of Claim 2**

The amendment of claim 2 removes the prior dependency of the claim upon a canceled base claim.

CONCLUSION

Applicants respectfully request entry of this amendment and continued examination of the application. Applicants submit that claims 2 and 17-36 are now in condition for allowance. The Commissioner is hereby authorized to charge any deficiency in fees to Deposit Account No. 23-0280. The undersigned invites the Examiner to call her to discuss any informalities that remain.

Respectfully submitted,

Date: Sept. 17, 2001

By: Judie D. Dziezak

Judie D. Dziezak, Reg. No. 40,599
Wallenstein & Wagner, Ltd.
311 South Wacker Drive, 53rd Floor
Chicago, Illinois 60606
Phone: (312) 554-3300
Attorneys for Applicants

JDD/hmp/130067.1

ATTACHMENT A – Marked-Up Claims

2. (Amended) A molecule [according to claim 1] comprising at least complement protein modules 1-4 [of complement factor H, or a molecule resulting from partial modification thereof, or an allelic mutant thereof] selected from the group consisting of complement control protein modules 1-4, 1-5, and 1-6 of complement factor H.

17. (Amended) A molecule comprising complement control protein modules, wherein said complement control protein modules are modules 1-4 of complement factor H.

18. (Amended) The molecule of claim 17 wherein the complement factor H is human complement factor H.

19. (Amended) The molecule according to claim 18, wherein the complement control protein modules 1-4 have the sequence of SEQ ID NO: 9.

22. (Amended) A [complement system inhibiting] molecule with complement inhibitory activity comprising complement control protein modules selected from the group consisting of only 1-4, 1-5, and 1-6 of complement factor H. (NM?)

23. (Amended) The molecule according to claim 22, the complement factor H being human complement factor H.